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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/991,588	11/21/2001	John Arnold Budny	1008-120.US	4312

7590 06/30/2004

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EXAMINER	
MITRA, RITA	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/991,588	BUDNY ET AL.	
	Examiner	Art Unit	
	Rita Mitra	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' response to the "Request for substitute papers" dated April 17, 2003, filed on April 25, 2003 is acknowledged. Claims 1-19 are currently pending and under examination. A telephone call was made to Attorney Colin Abrahams on April 9, 2004, to request an oral election of one sequence and one protein from claims 3 and 5. In response, an election of RGD type sequence; and osteonectin and SPARC protein from claims 3 and 5 was made. The remaining sequence and proteins from claims 3 and 5 are withdrawn from further consideration pursuant to 37 CFR 1.142 (b) as being drawn to non-elected inventions. At present there is no allowable generic or linking claim. Therefore, claims 1-19 and RGD type sequence; and osteonectin and SPARC protein are under examination.

The restriction requires a selection of a single amino acid sequence because each sequence has a different chemical and physical property (See specification pages 26-27). For example the peptide sequence RGDC (Arg-Gly-Asp-Cys) as set forth in SEQ ID NO: 1; while EILDVPST (Glu-Ile-Leu-Asp-Val-Pro-Ser-Thr) as set forth in SEQ ID NO: 20. In addition the invention also includes fragments and variants, which have different amino acid sequences, which are distinct from each other.

Objection to specification

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Claims 1 and 10 recite matrix selected from glycolic acid and lactic acid, while specification describes matrix selected from polymers of glycolic acid and lactic acid. A correction is suggested.

Objection to Claims

Claim 11 is objected to for using 2 periods at the end of line 3.

Claims 12 and 13 are objected for the term "biogradable at line 4," A correction to "biodegradable" would obviate this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-15, 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 10 and 11 are indefinite because of the use of the term "portion." The term "portion" renders the claim indefinite, it is not clear which portion of the matrix or matrix substrate where biologically active molecule is attached, whether it is N-terminal or C-terminal. Also it is not clear whether or not, a "portion" is or is not same for first and second biologically active molecules. Claims 2-9 and 12-15 are included in the rejection because they depend upon rejected claims and do not correct the deficiency of the claims from which they depend.

Claim 11 is indefinite because of the use of the term "capable." The claim is drawn to a composition for treating bone tissue comprising a matrix capable of forming a scaffold. The word "capable" is not clear, whether the matrix actually needs to form scaffold, or merely have the capability to do so. The word "capable" associates with the latent function only. Claims 12-15 are included in the rejection because they depend upon rejected claims and do not correct the deficiency of the claims from which they depend.

Claims 1, 9, 10 and 17 are indefinite because it is not clear what are the components of the combination and the amounts of each of the components in the combination. There are 3-4 members listed in the Markush group and the "combination thereof" is not a closed group, which is required of Markush groups. Claims 2-9 are also included in the rejection because they depend upon rejected claims and do not correct the deficiency of the claims from which they depend.

Claim 15 recites the limitation "the organic matrix" in last line. There is insufficient antecedent basis for this limitation in the claim.

Claims 18 and 19 are indefinite because they lack essential steps of administration as claimed in the method of treating bone tissue.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –
(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claim Rejections -35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murayama et al. (US Patent 5891192, Issue date April 6, 1999, Filing date May 22, 1997). Murayama et al. teach an intralumenal implant comprising an implant body of a biocompatible material and an ion-implanted protein coating on the body. The reference also teaches a method of making an ion-implanted protein-coated intralumenal implant comprising : a) providing an implant body of a biocompatible material, b) coating the body with a protein to form a protein coated body and c) subjecting the protein coated body to ion implantation (see col 2, lines 1-14). Murayama et al. also teach implant bodies may be made of bioabsorable or nonbioabsorable polymers or copolymers. Examples of bioabsorable polymers that have been used to make intralumenal implants are polygycolic acid, polygycolic acid/polylactic acid copolymers (see col 2, lines 40-45). The reference also teaches naturally occurring mammalian cell adhesion proteins containing one or more bonding sites (e.g., the RGD peptide sequence) that is recognized by receptors on various cell types such as platelets, fibroblasts, and endothelial cells. Examples of cell adhesion proteins are collagen, fibronectin, vitronectin, laminin and fibrinogen (see col 2, lines 64-67 to col 3, lines 1-4).

Thus, it would have been obvious to a person having ordinary skill in the art at the time applicant's invention was made to have used the teachings of Murayama et al., to have a composition comprising a matrix made of bioabsorable polymer like polyglycolic acid, polylactic acid and collagen, wherein biological active molecules fibronectin and vitronectin sharing an RGD type sequence are attached to the matrix (claims 1-5, 10-16). Murayma does not teach only two biological active molecules in the composition but the reference suggests that a mixture of cell adhesion proteins, eg. collagen, fibronectin , vitronectin, laminin and fibrinogen may be used for the coating of the intralumenal implant (col 3, lines 2-4). Therefore, a person of ordinary skill would be motivated to use a combination of fibronectin and vitronectin as in claim 1 of the instant application.

Claims 1-7 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murayama et al, in view of Brands et al. (EP 0587205A1, pp. 1-6, March 1994), taken with Kuberasampath et al. (US patent 5, 496,552, March 5, 1996).

Murayama et al. teach an intralumenal implant comprising an implant body of a biocompatible material and an ion-implanted protein coating on the body. The reference also teaches a method of making an ion-implanted protein-coated intralumenal implant comprising : a) providing an implant body of a biocompatible material, b) coating the body with a protein to form a protein coated body and c) subjecting the protein coated body to ion implantation (see col 2, lines 1-14). Murayama et al. also teach implant bodies may be made of bioabsorable or nonbioabsorable polymers or copolymers. Examples of bioabsorable polymers that have been used to make intralumenal implants are polygycolic acid, polygycolic acid/polylactic acid copolymers (see col 2, lines 40-45). The reference also teaches naturally occurring mammalian cell adhesion proteins containing one or more bonding sites (e.g., the RGD peptide sequence) that is recognized by receptors on various cell types such as platelets, fibroblasts, and endothelial cells. Examples of cell adhesion proteins are collagen, fibronectin, vitronectin, laminin and fibrinogen (see col 2, lines 64-67 to col 3, lines 1-4). Murayama does not teach a matrix where both fibronectin and vitronectin are attached to the matrix.

Brands et al. teach solid carriers for the attachment of cells which are coated with a polypeptide (preferably between 5 and 25 amino acids) containing the amino acid sequence Arg-Gly-Asp (see abstract), with a method for the preparation thereof (see page2, lines 1-3). The reference further teaches that the actual attachment of the cells are mediated by attachment factors that either can be synthesized by certain types of cell themselves or must be provided with the growth medium. These attachment factors, of which fibronectin and vitronectin are most known, share a common epitope consisting of a sequence of a three amino acids Arg-Gly-Asp. This epitope is recognized by a receptor (e.g. the fibronectin receptor) on the cell surface (see page 2, lines 10-13). Although the reference EP'205 does not disclose a matrix selected from the group consisting of glycolic acid, lactic acid, collagen and demineralized bone in the composition, in view of the fact that the reference teaches both the biologically active molecules fibronectin and vitronectin sharing an RGD type sequence (Arg-Gly-Asp) for coating a solid carrier for the attachment of cells, it would have been obvious to and motivated one of ordinary skill in the art to have combined the teachings with those of , e.g., Kuberasampath et al. in US '552. The reference '552 teaches osteogenic devices comprising a matrix containing substantially pure mammalian osteogenic protein and methods of inducing endochondral bone growth in mammals (see abstract), wherein the matrix is made up of particles or porous materials. The reference also teaches structuring as desired a material that is biocompatible and biodegradable in vivo

to serve as a "temporary scaffold" and substratum for recruitment of migratory progenitor cells, and as a base for their subsequent anchoring and proliferation (see col. 3). This addresses claims 12-16. The reference also teaches useful matrix materials, for example, collagen, homopolymers and copolymers of glycolic acid and lactic acid, demineralized bone etc.(see col. 3, lines 42-58). This addresses claims 1-11 of the present invention, wherein the matrix is selected from the group consisting of glycolic acid, lactic acid, collagen, demineralized bone or a combination thereof, while reference EP'205 teaches a matrix consisting of solid substrates e.g. glass or plastics or synthetic materials, e.g. microcarriers or macrocarriers. It would have been obvious to a person having ordinary skill in the art at the time applicant's invention was made to substitute the solid substrates e.g. glass or plastics or synthetic materials, e.g. microcarriers or macrocarriers of EP '205 with copolymers of glycolic acid and lactic acid of US'552. Reference US'552 also teaches a carrier which is biodegradable-synthetic or synthetic-inorganic matrix e.g. HAP, collagen, tricalcium phosphate, or polylactic acid and polyglycolic acid (col. 14, lines 56-59). This addresses claim 18, wherein the matrix is an inorganic matrix having a predetermined dissolution rate. Further the reference '552 teaches (see col 15, lines 11-20) a carrier that binds osteogenic protein (OP) and act as a slow release delivery system, accommodate each step of the cellular response during bone development, and protect the OP from nonspecific proteolysis. This addresses claim 16 of the present invention, wherein a composition for inhibiting proteolysis of extracellular matrix protein, comprising a biodegradable matrix forming a scaffold, and vitronectin attached to the matrix for release therefrom as the matrix degrades. Reference '552 also teaches the polylactic acid (PLA) and polyglycolic acid (PGA) and various combinations have different dissolution rates in vivo. This addresses composition of claim 14 wherein the matrix has a differential disappearance rate. It would have been obvious to a person having ordinary skill in the art at the time applicant's invention was made to substitute the solid substrates e.g. glass or plastics or synthetic materials, e.g. microcarriers or macrocarriers of EP '205 with the matrix of US'552.

The reference EP'205 further teaches that the polypeptide molecules of the formula (1) Xaa-Arg-Gly-Asp-Xaa can be cross-linked with the solid substrate e.g. using a bifunctional cross-linking agent such as SPDP(N-succinidimyl 3-(2-pyridyldithio)propionate), see page 2, lines 57-58. This addresses the bifunctional cross-linking agent of the instant application (claims 6, 7). The method of the preparation of the carriers of EP'205 reference addresses the method of making the composition of claim 10. Thus one skilled in the art recognizes the preventing a covalent linking of the polypeptide

molecule to the solid substrate of EP'205. One would be motivated to attach covalently the biologically active molecules, fibronectin and vitronectin of EP'205 to the porous matrix of US'552 to facilitate the adhesion of bone cells to the matrix (see col. 3, lines 45-55).

In view of the foregoing the claimed invention was *prima facie* obvious to make and use at the time it was made.

Conclusion

No claim is allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rita Mitra whose telephone number is (571) 272-0954. The Examiner can normally be reached from 9:30 a.m. to 6:30 p.m. on weekdays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Christopher Low, can be reached at (571) 272-0951. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (703) 872-9306. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0547.

Rita Mitra, Ph.D.
June 21, 2004

Jon P. Weber, Ph.D.
Primary Examiner